IN THE SPECIFICATION

Please add the following Abstract:

Please amend the title to read:

-- REPEATABLE SOFTWARE-BASED ACTIVE SIGNAL PROCESSING TECHNIQUE --.

Please amend the Specification as follows:

Please insert the following prior to the Field of the Invention:

- - Claim of Priority

This application is continuation of U.S. Pat. No. 09/913131, filed on August 8, 2001, which is a national stage application of PCT US00/04150 filed on February 17, 2000, which claims priority to U.S. Pat. App. No. Ser. No. 09/253,792, filed on February 22, 1999, now U.S. Pat. No. 6,142,681 - -.

Please amend the paragraph on page 3, lines 2-26 as follows:

> One analysis technique for achieving the aforementioned advantages is described in co-pending U.S. Patent Application 09/253,789, now U.S. Pat. No. 6,136,541, filed contemporaneously herewith, entitled "Method and Apparatus for Interpreting Hybridized Biochip Patterns Using Resonant Interactions Employing Quantum Expressor Functions", (the "co-pending application") and incorporated by reference herein. Briefly, the method of the co-pending application operates as follows. The method identifies mutations, if any, present in a biological sample from a set of known mutations by analyzing a dot spectrogram representative of quantized hybridization activity of oligonucleotides in the biological sample to identify the mutations. A resonance pattern is generated which is representative of resonances between a stimulus pattern associated with the set of known mutations and the dot spectrogram. The resonance pattern is interpreted to yield a set of confirmed mutations by comparing resonances found therein with predetermined resonances expected for the selected set of mutations. In a particular example described in the co-pending application, the resonance pattern

is generated by iteratively processing the dot spectrogram by performing a convergent reverberation to yield a resonance pattern representative of resonances between a predetermined set of selected Quantum Expressor Functions and the dot spectrogram until a predetermined degree of convergence is achieved between the resonances found in the resonance pattern and resonances expected for the set of mutations. The resonance pattern is then analyzed to ~~a~~ yield a set of confirmed mutations by mapping the confirmed mutations to known diseases associated with the pre-selected set of known mutations to identify diseases, if any, indicated by the DNA sample. A diagnostic confirmation is then made by taking the identified diseases and solving in reverse for the associated Quantum Expressor Functions and then comparing those Quantum Expressor Functions with ones expected for the mutations associated with the identified disease to verify correspondence. If no correspondence is found, a new sub-set of known mutations are selected and the steps are repeated to determine whether any of the new set of mutations are present in the sample.

Please amend the paragraph on page 3, lines 27-33 as follows:

By exploiting a resonant interaction, mutation signatures may be identified within a dot spectrogram even in circumstances involving low signal to noise ratios or, in some cases, negative signal to noise ratios. By permitting the mutation signatures to be identified ~~is~~ in such circumstances, the reliability of dot spectrogram analysis is thereby greatly enhanced. With an increase in reliability, costs associated with performing the analysis are decreased, in part, because there is less of a ~~require-ment~~ requirement for skilled technicians. Other advantages of the invention arise as well.

Please amend the paragraph on page 7, lines 10-11 as follows:

FIG. 4-A is a first portion of a flowchart illustrating an exemplary method for analyzing the output of a hybridized DNA microarray in accordance with the method of the present invention

FIG. 4-B is a second portion of flowchart illustrating an exemplary method for analyzing the output of a hybridized DNA microarray in accordance with the method of the present invention.

FIG. 4-C is a third portion of flowchart illustrating an exemplary method for analyzing the output of a hybridized DNA microarray in accordance with the method of the present invention.

Please amend the paragraph on page 8, lines 17-21 as follows:

Hence key components of the exemplary biomolecular detection method of the co-pending application are: (i) selection of a basis system; (ii) generation of designer Quantum Expressor Function (QEF) for coupling with the substrate to be analyzed; (iii) generation of a Hamiltonian to describe relaxation dynamics of the coupled system; (iv) modulation of resonance parameters to enforce early resonance; (v) and exploitation of resonance suppressors to verify detection.

Please amend the paragraph on page 10, lines 17-22 as follows:

Referring now to FIGS. 4-A - 4C, initially at step 300, a set of mutations of interest are selected and at step 301 preconditioner transforms are generated based upon the selected set of mutations. At step 302, Quantum Expressor Functions are generated based upon the Hamiltonian of a pre-selected basis system. Phase shifted resonance stimulus is generated, at step 304, using the Quantum Expressor functions. Grouping stimulus is also generated, at step 305.

Please amend the paragraph on page 11, lines 4-15 as follows:

The actual resonant interaction, which involves convergent reverberations, includes the following sub-steps also shown in FIGS. 4A - 4C. At step 316, a resonance dynamics iteration is initiated which includes the use of ensemble boundary and CSR operators (step 318) and the use of bulk property estimators (step 320). The ensemble boundary filters, CSR filters and bulk property estimators are applied to the tessellated, re-normalized dot spectrogram in combination with the resonance and group stimulus. The resulting filtered dot spectrogram is then evaluated to determine a degree of resonance convergence to one or more of the set of predetermined mutations, at step 322. The degree of convergence is evaluated, at step 324, against a Lindbald condition and, if the Lindbald condition is not met, the system is deemed to be subject to paralysis of dynamics and execution proceeds to step 326 wherein possible hixel death is compensated for by increasing a time scale for the iteration initiated at step 316 and then repeating the iteration.

Please amend the paragraph on page 13, lines 26-29 as follows:

The selection of the basis system and the generation of the QEF's based thereon depends, in part, and the ~~characteristies~~ characteristics of the DNA microarray. In the exemplary embodiment, the DNA microarray is an ~~N by M~~ *N* by *M* DNA chip array wherein an element of the array is referred to herein as an *"oxel": o(i,j)*.

Please amend the paragraph on page 15, lines 6-12 as follows:

Typically, in signal processing applications, high pass or band pass spatial filtering is implemented to enhance SNR in DS matrix. Alternate methods apply a combination of Laplacian or other edge detection filters ~~apply~~ to enhance signal from arrays cells with a higher hybridization concentration from those of the adjacent cells. These SNR enhancement methods however work only with positive or zero-SNR. Since SNR in general is negative in our case (ultra-low target DNA concentrations), these methods in effect amplify noise or further blur the hixel boundaries.

Please amend the paragraph on page 15, lines 20-27 as follows:

The parametric of most interest is the integrated density of states, given by

$$N(\lambda) = \operatorname*{Lim}_{L\to\infty} \frac{1}{\pi \mathrm{L}} E\{\aleph(L)\}$$

where $\aleph' = \sqrt{\lambda} - \frac{q}{\sqrt{\lambda}} \sin^2 \aleph$

whence

$$\aleph' \Big|_{\aleph = \pi n} = \sqrt{\lambda} > 0$$

~~where n~~ where N is the number of eigenvalues to the system (random field approximation).

Please amend the paragraph on page 15, lines 30-33 as follows:

Amplitude wandering is determined using Palm generators as described in the co-pending patent #~~1~~ application. The Palm generators exploits the notion of generator functions to capture stochastic variability in hybridization binding efficacy. The exemplary method described herein draws upon results in stochastic integral geometry and geometric probability theory.

Please amend the paragraph on page 16, lines 1-16 as follows:

"Amplitude wandering estimate" that bounds the hixel amplitude dispersion due to total hybridization losses, is computed using Palm generators over the globally re-scaled dot spectrogram to capture amplitude wanderings and transitions at element, neighboring pair and local ensemble levels. Step 310 provides a measure for each mutation-recognizer centered (MRC-) hixel that is invariant to local degradation. The measure is expressed via the form

$$m(Z) = \int_Z f(z)dz$$

where Z denotes the set of mutations of interest. In other words, we determine the function ~~f(z)~~ $\underline{f}\,\underline{(z)}$ under the condition that ~~m(z)~~ $\underline{m(Z)}$ should be invariant with respect to all dispersions ξ. Also, up to a constant factor, this measure is the only one which is invariant under a group of motions in a plane. In principle, we derive deterministic analytical transformations on each MRC-hixel., that map error-elliptic dispersion bound defined on $\Re^2$ (the two dimension Euclidean space - i.e., oxel layout) onto measures defined on $\Re$. The dispersion bound is given by the form

$$\mathrm{Log}_4(\hat{O}_{(i,j)}\,|^{Z}).$$

Please amend the paragraph on page 16, lines 18-28 as follows:

Recall that Palm distribution, Π of a translation (T_n) invariant, finite intensity point process in $\Re^n$ is defined to the conditional distribution of the process. It is expressed in terms of a Lebesgue factorization: $E_P N^* = \Lambda L_N X \Pi$, where Π and Λ completely and uniquely determine the source distribution P of the translation invariant point process. The term $E_P N^*$ denotes the first moment measure of the point process and L_N is a probability measure. In ~~patent #1~~ the co-pending application we described how to compute Π and Λ which can uniquely encode the dispersion and amplitude wandering associated with the MRC-hixel.

Please amend the paragraph on page 20, lines 11-12 as follows:

The above expression provides an estimate of when a ~~geomteric~~ geometric motion embodied by the convolutionless equation, is no longer a plausible resonance candidate.

Please amend the paragraph on page 24, lines 8-11 as follows:

The technique described with respect to FIGS. 4-A – 4-C is particularly powerful in that it provides an enumerative solution which generally covers all possible diagnostic candidates as opposed to only one or two, given the best genomic understanding or mapping between expressed genes and diseases.

Please amend the paragraph on page 24, lines 14-17 as follows:

Details regarding an implementation directed to measuring viral loads may be found in co-pending U.S. Patent Application 09/253,791, now U.S. Pat. No. 6,235,511, also filed contemporaneously herewith, entitled "Exponentially Convergent Therapy Effectiveness Monitoring Using Viral Load Measurements", and also incorporated by reference herein.

Respectfully submitted

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I hereby certify that this correspondence (along with any paper referred to as being attached or enclosed) is being sent via overnight express mail on October 2, 2003.

Dated: 10-1-2003

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